

including HOA subtypes, disease severity, disease duration, number of joints involved, affected site, age of patients, and occupational activities. According with the EULAR recommendations three treatment modalities can be proposed: non-pharmacological, pharmacological, and surgical. In many patients these modalities should be combined, tailored to individual needs and risk factors.

Although non-pharmacological therapies are important in the management of HOA, high quality evidence is lacking. The exercise seems useful when combined with education and joint protection. Advice regarding the use of electrotherapy, thermotherapy, ultrasound, TENS or laser therapy is conflicting, mainly due to the lack of eligible studies. So, their inclusion in recommendations relies mainly on consensus methods and expert opinion.

As regard as the pharmacological therapy, the most realistic aim is the pain relief, due to limited evidence of reliable efficacy in modifying disease activity by drugs.

Among analgesics, paracetamol is considered as the first choice and, if successful, the preferred for long term, although evidence supporting its use in HOA are few. In mild to moderate pain and when not many joints are affected, topical treatments are a good option for many aspects, including the cost effectiveness. If paracetamol or topical NSAIDs are insufficient, then the addition of opioid analgesics should be considered, although the evidence supporting its use in HOA is poor.

In patients who respond inadequately to paracetamol or topical treatments, oral NSAIDs or COX-2 inhibitor should be used in substitution or in addition, possibly at lowest effective dose for the shortest period of time and taking into account individual patient risk factors, including age and comedications.

Intra-articular (IA) long-acting corticosteroid is effective for painful flares of OA, especially trapeziometacarpal joint (TMC) OA and so, it should be considered as an adjunct to core treatment for the relief of moderate to severe pain in people with HOA. There are contrasting opinions on the usefulness of IA hyaluronan (HA) in all existing recommendations. However, in two recent trials it seems more favourable than IA steroids.

The most studied SYSADOA in HOA has been the chondroitin sulphate (CS). In the recent 6 months RCT performed by Gabay, decrease in global hand pain and improvement of hand function were significantly more pronounced in the CS than in the placebo group. This drug was also evaluated as DMOAD, in two independent trials comparing CS with placebo and chondroitin polysulphate (CPS) with placebo in erosive HOA (EHOA). The results showed that over a 3-year period CS was no more beneficial than placebo, whereas CPS was more effective than placebo in preventing radiographic progression.

The EHOA is the HOA subset deserving main attention by new treatment strategies, due to its severity and poor outcome. So, anti-cytokines biologic agents have been tested in some pilot studies using s.c. anakinra, humira and IA infliximab, with good results, as also confirmed by the first RCT recently performed by Verbruggen, with Humira.

Surgery is uncommonly performed in HOA, and evidence for its effectiveness is lacking. However, for HOA at the base of the thumb, evidence does support effectiveness of surgical therapy when conventional therapies have failed. These surgical interventions include trapeziectomy, arthrodesis, osteotomy, ligament reconstruction, and joint replacement. Surgery for areas other than the thumb base is not yet widely available as a treatment option.

I-23

PATHOPHYSIOLOGY OF POST-TRAUMATIC ARTHRITIS

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Epidemiologic studies have firmly established the association between acute joint injury and the increased risk for the subsequent development and progression of osteoarthritis (OA). All of the joint tissues are susceptible to traumatic injury, including the ligaments, menisci, articular cartilage and periarticular bone, and to some extent the natural history of the OA process is related to the magnitude, site and extent of the initial joint injury. However, independent of the specific site or target tissue affected by the injury, all of the joint tissues are eventually affected by the osteoarthritic process. Multiple mechanisms contribute to the pathogenesis of the osteoarthritic changes after a joint injury and although much of the attention has focused on the adverse effects of increased joint instability and altered joint mechanics, there is evidence that the pathogenic process in many individual is in fact attributable to the initial acute-impact injury to the articular surface

and in some instances the adjacent subchondral bone. These impact injuries not only may disrupt the structural integrity of these tissues but also can induce acute as well as chronic adverse effects on the survival and functional activities of the resident cell populations. With respect to the articular cartilage these changes include de-regulation of the synthetic and reparative capacity of the chondrocytes, as well as the release of potent biological mediators such as reactive oxygen species, proteolytic enzymes and proinflammatory cytokines. In addition, although OA generally is not viewed as an inflammatory form of arthritis there is evidence that synovial inflammation not only contributes to joint symptoms but also plays a role in the structural and functional deterioration of joint tissues in both post traumatic OA and other forms of OA. De-regulated chondrocyte function and the release of biologically active chondrocyte-derived factors or products from the cartilage extracellular matrix have been implicated in the synovial inflammation, and many of the synovial derived products in turn may adversely affect the homeostasis of the adjacent articular cartilage and bone. Studies have shown that the risk factors for OA initiation and progression in patients with post traumatic OA are similar to those for idiopathic OA in that systemic host factors and local biomechanical factors interact and that obesity, female gender, and pre-existing early-stage OA contribute significantly to adverse radiographic and clinical outcomes. There remains uncertainty regarding the long-term benefit of surgical interventions with respect to prevention or slowing the development of OA, and there is a critical need for rigorous clinical and laboratory studies to define the factors that are responsible for joint deterioration in patients with traumatic joint injuries and for assessing the impact of interventions on the status of joint tissues and function.

I-24

REGENERATIVE MEDICINE APPROACHES FOR THE TREATMENT AND PREVENTION OF OSTEOARTHRITIS

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Osteoarthritis (OA) is the most common joint disease and is estimated to affect more than 8 million people in the UK alone. Underlying the disease is a loss of the normal homeostasis of the joint with progressive breakdown of tissues including articular cartilage and subchondral bone leading to end-stage joint destruction and failure. For the patient, quality of life is reduced because of the loss of movement and joint pain increases to become continuous, even at rest. OA is defined as a complex disorder with three groups of risk factors: genetic, constitutional (e.g., ageing and obesity) and local (e.g., secondary to mechanical load and joint injury).

Current treatment options are limited to analgesia and physiotherapy, and to prosthetic joint replacement for end-stage disease. Management of OA is aimed at alleviating symptoms but current treatments do not address the disease process itself. There is an unmet need to develop new treatment options that could halt disease progression, at an early stage. In this respect, regenerative medicine (including tissue engineering) offers the potential for a long-term solution via biological regeneration, repair or replacement of the degenerate joint tissues. Pioneering approaches to biological joint resurfacing include autologous chondrocyte implantation and marrow stimulation techniques such as microfracture. The lecture will outline possible cell-based therapy interventions to treatment or prevention of OA, with a particular focus onto secondary post-traumatic OA. Exogenous (autologous or allogeneic) stem cells could be injected intra-articularly into affected joints or implanted locally into a damaged tissue, for instance into a defect of the articular cartilage, either in suspension or in combination with a biomaterial. Stem cells could be transplanted either after culture-expansion or as minimally manipulated, e.g. immediately after their purification from their tissue sources. However, important ongoing issues relate to identity characterization and potency assessment of the different types of stem cells and how they can be bioprocessed with consistency and implanted for effective repair of the damaged joint surface and degenerate joint tissues. Using stem cells in combination with biomaterials, there is also the potential to create ex vivo biological joint tissues such as menisci, or even a fully biological prosthesis. Opportunities and challenges from a research perspective will be discussed.

The arthritic joint also demonstrates apparent repair mechanisms that can result in aberrant formation of cartilage and bone in the form of chondro-osteophytes. This presumes existence of endogenous stem cells in the joint. In this regard, we recently provided data on the

identification and characterization of endogenous resident mesenchymal stem cells (MSCs) in the adult mouse knee joint synovium *in vivo*. Currently, we are investigating the role of the endogenous MSCs in the mechanisms underlying joint homeostasis as well as development and progression of OA. The existence of functional MSC niches in the adult joint opens up unprecedented opportunities for pharmacological interventions by using medications that would target MSC niches and related reparative signalling pathways to activate and modulate intrinsic mechanisms of joint tissue regeneration. It is hoped that such interventions may halt progression of OA or even prevent OA, while restoring an effective homeostatic joint.

I-25 YEAR IN REVIEW: CLINICAL

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Purpose: To review important articles published since the 2011 World Congress of Osteoarthritis in the clinical and epidemiologic areas of osteoarthritis (OA).

Methods: A systematic review of the literature was conducted. Medline was searched through PubMed using the search terms “osteoarthritis [ti]”. The search was restricted to English language, humans and all adults age 19+ for the time period “last 180 days.” The search was further limited by adding the word “clinical.”

Results: A total of 118 and 42 titles were identified in the initial and restricted searches, respectively. The author reviewed the titles of the 42 articles and chose several that will be briefly discussed during his presentation.

Conclusions: There have been some important clinical and epidemiologic studies of OA that have been published since the 2011 World Congress of OA. The search will be updated in the weeks just prior to the 2012 World Congress in order to identify and highlight newer literature.

I-26 OSTEOARTHRITIS YEAR IN REVIEW: REHABILITATION AND OUTCOMES

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Purpose: This review highlights seminal publications of rehabilitation and outcomes in osteoarthritis (OA) of the hip or knee.

Methods: A systematic literature search was performed in Medline from July 2011 up to January 24, 2012 using the terms ‘osteoarthritis, knee’, ‘osteoarthritis, hip’ rehabilitation, physical therapy, exercise and preoperative intervention, outcomes. Trials evaluating rehabilitation interventions were included if they were randomized trials (RCT) or systematic reviews. Surgical interventions and pharmacology studies were excluded unless they included evaluation of a rehabilitation intervention. Outcome studies were included if they contributed methodologically to advancing outcome measurement.

Results: The literature search identified 259 hits. 21 publications were selected and reviewed that related to cost-effectiveness of non-pharmacological and non-surgical interventions, interventions evaluating care processes, decision making and information, weight loss, exercise (balance training, walking, neuromuscular, combined with self-management, aquatic vs. landbased, adherence), bracing, whole body vibration, short wave therapy and acupuncture/moxibustion. One systematic review provided limited evidence for the cost-effectiveness of conservative treatments for the management of hip and/or knee osteoarthritis. This was supported by a large RCT showing patients randomized to exercise and self-management having a high probability of being cost-effective at 30 months.

Another meta-analysis found low to moderate evidence from mostly small RCTs demonstrating that pre-operative interventions, particularly exercise, reduce pain for patients with hip and knee osteoarthritis prior to joint replacement, and exercise with education programs may improve activity after hip replacement.

The increased focus on care strategies, decision-making instruments and patient information in osteoarthritis treatment was highlighted by several publications. A consensus-based strategy provided a framework for health care providers and patients with hip or knee osteoarthritis to discuss the optimal timing of the various treatment options. An audiovisual patient decision aid aiming at changing disadvantageous beliefs and encourage physical activity was associated with a small effect.

The studies on exercise added information on treatment effect of important aspects such as type, combined treatments, and adherence to exercise.

A single high quality RCT found low-energy-diet induced weight loss to relieve pain also at one year and lead to independent losses of leg muscle tissue and strength, indicating the need for exercise in conjunction with low-energy-diet induced weight loss programs.

A systematic review failed to provide conclusive evidence for the effectiveness of moxibustion (warm acupuncture) compared with drug therapy in rheumatic conditions. The total number of RCTs included in this review and their methodological quality were low. An RCT found moxibustion combined with intra-articular injection of sodium hyaluronate to be more effective than intra-articular injection of sodium hyaluronate alone. A secondary analysis of 10 000 patients included in one of four RCTs for one of four chronic pain problems, including hip or knee osteoarthritis, found that age, education, duration of illness, baseline pain, and some concomitant diseases predicted treatment outcome in both groups (routine care with or without acupuncture). Patients' characteristics that enlarged the acupuncture effect were being female, living in a multi-person household, failure of other therapies before the study, and former positive acupuncture experience.

A single high quality RCT among persons with symptomatic lateral PF OA found the effects of a specific realigning PF brace not to be of clinical or statistical significance.

One RCT found pulsed shortwave treatment to be an effective method for pain relief and improvement of function and quality of life in the short term in women with knee OA.

The 16 outcomes papers considered relevant did not add significantly to current knowledge.

Conclusion: The current clinical focus on non-pharmacological and non-surgical treatment of hip or knee OA translates into research findings that increasingly are included in meta-analysis improving the evidence level for non-pharmacological and non-surgical treatments in hip or knee OA. Information, exercise and weight loss are supported as first line treatments and as adjunctive treatments prior to surgery.

I-27 YEAR IN REVIEW – BIOLOGY

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An overview will be given on selected topics that have advanced our understanding of the (patho)biology of osteoarthritis. More and more it becomes clear that osteoarthritis is not a cartilage-only disease but that all joint tissues are involved and contribute to the overall disease process. Osteoarthritis is an affliction of the whole joint. In addition to cartilage, attention will be paid to other tissues such as the synovium. The role of cellular communication, inflammatory mediators, for instance components of the complement system, and the role of miRNA will be addressed.

I-28 YEAR IN REVIEW: BIOMARKERS

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Purpose: Biomarkers have the capacity to detect cartilage degradation in degenerative joint diseases such as osteoarthritis (OA). They can provide useful diagnostic information by reflecting disease relevant biological activity in the joint and predict the course of disease progression. In addition, they can serve as surrogate endpoints in the drug discovery process. The “Year in Review” Plenary Session at the end of the World Congress on Osteoarthritis is becoming a well-established tradition. It provides a unique opportunity to build on the reviews from the previous two years and summarize the key published papers related to OA biomarkers. This presentation reviews the biomarker papers published between the OARSI 2011 Congress held from 15–18 September 2011 in San Diego, California and the OARSI 2012 meeting, which will be held from 26–29 April 2012 in Barcelona, Spain.

Methods: The PubMed/MEDLINE and SciVerse Scopus bibliographic databases were searched using the following keywords: ‘biomarker’ and ‘osteoarthritis’. The PubMed/MEDLINE literature search was conducted using the Advanced Search Builder function (<http://www.ncbi.nlm.nih.gov/pubmed/advanced>) and specifically focused on the eight months between the 2011 and 2012 meetings.

Results: Approximately thirty-two new OA biomarker papers were published at the time this abstract was written (February 14, 2012). It is estimated that fifty papers will be published by April 2012. Some of